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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/226,794	01/07/99	DEBINSKI	W 6460-4

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EXAMINER	
UNGAR, S	
ART UNIT	**PAPER NUMBER**
1642	15

DATE MAILED: 05/08/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/226,794	Debrinski et al
Examiner	**Art Unit**
Ungar	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 13, 2001*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, and 4-13* is/are pending in the application.

4a) Of the above, claim(s) *7-13* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, and 4-6* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

1. .The request filed on April 13, 2001 (Paper No. 14) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/226,794 is acceptable and a CPA has been established. An action on the CPA follows.

2 The Claims 1-2 and 4-6 are pending and currently under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Because all claims are drawn to the same invention claimed in parent application Serial No. 09/226,794 and no additional arguments or amendments to the claims have been submitted, claims 1, 2 and 4-6 remain rejected for the reasons previously disclosed in Paper No. 12, mailed November 13, 2000 as follows:

5. The following rejections are being maintained:

Double Patenting

6. Claims 1 and 4-5 remain rejected under the judicially created doctrine of obviousness-type double patenting for the reasons previously set forth in Paper No. 9, Section 4, pages 2-4.

Applicant argues that (a) the current claims are not generic to the claims of the US Patent No. 5,614,191, that is they do not read on claims 14 and 16-20 of said patent because claim 20 does not necessarily include a step of delivering a molecule into a subject and (b) the description of the '191 patent does not disclose an experiment showing administration of a molecule having an IL-13 moiety which inhibits the growth rate of a tumor located within an animal, © to make an obviousnessness-type double patenting rejection, it must be shown that one of

ordinary skill in the art at the time the invention was made would have reasonably expected the claimed invention to work and because only *in vitro* experiments are disclosed in the disclosure, the patent as issued is not enabling because without an *in vivo* demonstration of efficacy, based on the information in the patent as issued, although it would have been obvious to try to reduce the growth rate of a tumor in an animal, there would be no expectation of success. The arguments have been considered but have not been found persuasive because (a') the current claims clearly read on the patented claims because both the patented claims and the claims of the instant invention are drawn to a method of reducing the rate of tumor cell growth *in vivo*. The patent clearly claims a method for "impairing growth of a solid tumor cell..... in a human". It is clear that impairing the growth of a solid tumor cell will reduce the rate of the tumor cell growth. Although the cited patent claims do not recite a step of administering the chimeric molecule *in vivo*, since the method is specifically drawn to impairing growth of a solid tumor cell growth in a human, it is clear and one of ordinary skill in the art would instantly envision that the chimeric molecule must be administered *in vivo*. There is no other way to impair growth of a solid tumor cell in a human, (b') the instant double-patenting rejection is based on the claims as issued, (c') it appears that Applicant is arguing that the issued patent is invalid because it is not enabling. It is presumed that a United States patent is valid unless it is overturned by the courts. Since the patent has not been overturned by the courts, it is presumed that the claims are valid as issued. Since the claims are valid, they are enabled. Applicant's arguments have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 102

7. Claims 1 and 4-5 remain rejected under 35 USC 102(b) for the reasons previously set forth in Paper No. 9, Section 8, pages 5-6.

Applicant argues that (a) a claim is anticipated only if each and every element as set forth in the claim is found either expressly or inherently described in a single prior art reference and that the '191 patent does not disclose a method comprising the step of delivering into the subject a molecule having an IL13-moiety and a cytotoxic moiety in an amount effective to reduce the growth of tumor cells, (b) the '191 patent is not enabling because no *in vivo* data was presented.

The arguments have been considered but have not been found persuasive because (a') although the cited patent claims do not recite a step of administering the chimeric molecule *in vivo*, since the method is specifically drawn to impairing growth of a solid tumor cell growth in a human, it is clear and one of ordinary skill in the art would instantly envision that the chimeric molecule must be administered *in vivo*, thus it is clear that the administration step is inherently described in the method as claimed in the prior art reference, (b') it appears that Applicant is arguing that the issued patent is invalid because it is not enabling. It is presumed that a United Stated patent is valid unless it is overturned by the courts. Since the patent has not been overturned by the courts, it is presumed that the claims are valid as issued. Since the claims are valid, they are enabled.

8. Claims 1, 2 and 4-5 remain rejected under 35 USC 102(a) for the reasons previously set forth in Paper No. 9, Section 9, pages 6-7.

Applicant argues that the abstract is non-enabling because there is no teaching of dosage, regimen method of delivery, method of implanting the tumor or its localization, nor does the reference mention the form of IL13-based cytotoxin.

The argument has been considered but has not been found persuasive because given the information that IL-13 expressing gliobastoma multiforme cells express large numbers of receptor for IL13 and that IL13/cytotoxin was effective in curing a high percent of mice bearing intracranial xenografts comprising this type of cells, it was well within the skill of those in the art using convention techniques, at the time the Abstract was published, to use the method even without specific instructions as to dosage, methods of delivery or the form of IL13-based cytotoxin. Applicant's arguments have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

9. Claims 1 and 6 remain rejected under 35 USC 103 for the reasons previously set forth in paper No. 9, Section 11, page 8.

Applicant argues that (a) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference or to combine reference teachings and there must be a reasonable expectation of success, (b) the Office Action does not indicate that claimed techniques would have had a reasonable expectation of success in view of the '191 patent or the Debinski et al abstract.

The arguments have been considered but have not been found persuasive because (a') the knowledge that intratumoral injection was conventional in the art at the time the invention was made was knowledge that was generally available and

further, since the method was conventional at the time the invention was made there was a reasonable expectation of success, (b') as stated above, the issued claims of a United States patent are valid and enabled and for the reasons set forth above, the Debinski et al abstract is enabling. Applicant's arguments have not been found persuasive and the rejection is maintained.

10. Claims 1-5 remain rejected under 35 USC 103 for the reasons previously set forth in paper No. 9, Section 12, pages 8-9.

Applicant argues that (a) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference or to combine reference teachings and there must be a reasonable expectation of success, (b) the Office Action does not indicate that claimed techniques would have had a reasonable expectation of success in view of the '191 patent or the Debinski et al reference, © the cited references, even in combination, did not teach how to practice the claimed method and did not provide a reasonable expectation of success. The arguments have been considered but have not been found persuasive because (a') and (c') clearly a method for impairing growth of a solid tumor cell bearing an IL-13 receptor by administering an IL-13 targeting molecule and an effector molecule in a human was well known in the art at the time the invention was made as claimed by US Patent No. 5,614,191 and that human glioblastoma multiforme tumor cells are extremely sensitive to a chimeric protein composed of hIL13 and a cytotoxin, PE38QQR as taught by Debinski et al. For the reasons previously set forth, the combined references teach not only the suggestion but also the means and motivation to

successfully reduce the rate of growth of tumor cells *in vivo* in a mammalian subject comprising an IL13-specific receptor comprising delivering into the subject a molecule having an IL13-moiety and a cytotoxic moiety in an amount effective to reduce the rate of growth of said tumor. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981), (b') and (c') given the teachings of the combined references, one would clearly have a reasonable expectation of success for the reasons previously set forth. Applicant's arguments have not been found persuasive and the rejection is maintained.

11. All other objections and rejections recited in Paper No. 9 are withdrawn.

12. No claims allowed.

13. This is a CPA of applicant's earlier application S.N. 009/226,794. All claims are drawn to the same invention claimed in the earlier application and, although applicant has filed request for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d), no Amendment or Response containing either arguments drawn to the instant rejections or amendments to the claims has been submitted. Thus, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). See M.P.E.P. § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this

application, all further correspondence regarding this application should be directed to Group Art Unit 1640.

Susan Ungar
Primary Patent Examiner
May 7, 2001